**Electronically Filed**

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| **APPELLANTS' BRIEF** | Attorney Docket No. | STAN-010CON2 |
| | Confirmation No. | 3761 |
| | First Named Inventor | Stanley Cohen |
| | Application Number | 10/697,720 |
| | Filing Date | October 29, 2003 |
| Mail Stop APPEAL<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, VA 22313-1450 | Group Art Unit | 1642 |
| | Examiner Name | Yu, Misook |
| | Title: "Mammalian Tumor Susceptibility Genes and their Uses" | |

Sir:

This Brief is filed in support of Appellants' appeal from the Examiner's Rejection dated August 4, 2009. No claims have been allowed. Claims 29-34 are pending, Claims 31-34 have been withdrawn from consideration. Claims 1-28 are canceled. The rejection of Claims 29-34 is appealed. A Notice of Appeal was filed on December 4, 2009. The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134(a).

The Commissioner is hereby authorized to charge deposit account number 50-0815, reference no. STAN-010CON2 to cover any required fee for filing the Applicant's brief. Additionally, in the event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, the Appellant petitions for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to the above disclosed deposit account.

## I. REAL PARTY IN INTEREST

The inventors named on this patent application assigned their entire rights to the invention to the Board of Trustees of the Leland Stanford Junior University.

## II. RELATED APPEALS AND INTERFERENCES

There are currently no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

## III. STATUS OF CLAIMS

The present application was filed on October 29, 2003 with a preliminary amendment canceling Claims 1-23 and presenting new claims 24-28. During the course of prosecution, Claims 1-28 were canceled, and Claims 31-34 were added. Accordingly, Claims 31-34 are pending in the present application, of which Claims 29-30 stand rejected and are appealed herein.

## IV. STATUS OF AMENDMENTS

Claim 29 was canceled and Claim 30 was amended in Applicants response to Final Office Action of October 21, 2009. The Advisory Action of December 4, 2008 indicated that the amendments would not be entered, and thus the claims stand as presented in the prior amendment, dated April 14, 2009. No further amendments have been made to the claims.

## V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is drawn to polypeptide compositions.

Claim 29 recites "an isolated polypeptide comprising the sequence of amino acid residues 11-390 of SEQ ID NO:4", and Claim 30 to a polypeptide "comprising the sequence of amino acid residues 11-390 of SEQ ID NO:4, free of other proteins and other cellular debris". The sequence identifier "SEQ ID NO:4" corresponds to the protein identified in the specification as human TSG101. The specification describes at page 7, line 8, the normal sequence of human TSG101 as provided by SEQ ID NO:3. The protein product of this genetic sequence is set forth in SEQ ID NO:4.

The sequence alignment pasted in below shows the relationship between the DNA sequence and the protein sequence:

(SEQ ID NO:3)

```
gaagggtgtg cgattgtgtg ggacggtctg gggcagccca gcagcggctg accctctgcc 60
tgcggggaag ggagtcgcca ggcggccgtc atg gcg gtg tcg gag agc cag ctc 114
                              Met Ala Val Ser Glu Ser Gln Leu
                               1               5

aag aaa atg gtg tcc aag tac aaa tac aga gac cta act gta cgt gaa 162
Lys Lys Met Val Ser Lys Tyr Lys Tyr Arg Asp Leu Thr Val Arg Glu
     10                  15                  20

act gtc aat gtt att act cta tac aaa gat ctc aaa cct gtt ttg gat 210
Thr Val Asn Val Ile Thr Leu Tyr Lys Asp Leu Lys Pro Val Leu Asp
 25                  30                  35                  40

tca tat gtt ttt aac gat ggc agt tcc agg gaa cta atg aac ctc act 258
Ser Tyr Val Phe Asn Asp Gly Ser Ser Arg Glu Leu Met Asn Leu Thr
                 45                  50                  55

gga aca atc cct gtg cct tat aga ggt aat aca tac aat att cca ata 306
Gly Thr Ile Pro Val Pro Tyr Arg Gly Asn Thr Tyr Asn Ile Pro Ile
             60                  65                  70

tgc cta tgg cta ctg gac aca tac cca tat aat ccc cct atc tgt ttt 354
Cys Leu Trp Leu Leu Asp Thr Tyr Pro Tyr Asn Pro Pro Ile Cys Phe
         75                  80                  85

gtt aag cct act agt tca atg act att aaa aca gga aag cat gtt gat 402
Val Lys Pro Thr Ser Ser Met Thr Ile Lys Thr Gly Lys His Val Asp
     90                  95                 100

gca aat ggg aag ata tat ctt cct tat cta cat gaa tgg aaa cac cca 450
Ala Asn Gly Lys Ile Tyr Leu Pro Tyr Leu His Glu Trp Lys His Pro
105                 110                 115                 120

cag tca gac ttg ttg ggg ctt att cag gtc atg att gtg gta ttt gga 498
Gln Ser Asp Leu Leu Gly Leu Ile Gln Val Met Ile Val Val Phe Gly
                125                 130                 135

gat gaa cct cca gtc ttc tct cgt cct att tcg gca tcc tat ccg cca 546
Asp Glu Pro Pro Val Phe Ser Arg Pro Ile Ser Ala Ser Tyr Pro Pro
            140                 145                 150

tac cag gca acg ggg cca cca aat act tcc tac atg cca ggc atg cca 594
Tyr Gln Ala Thr Gly Pro Pro Asn Thr Ser Tyr Met Pro Gly Met Pro
        155                 160                 165

ggt gga atc tct cca tac cca tcc gga tac cct ccc aat ccc agt ggt 642
Gly Gly Ile Ser Pro Tyr Pro Ser Gly Tyr Pro Pro Asn Pro Ser Gly
    170                 175                 180

tac cca ggc tgt cct tac cca cct ggt ggt cca tat cct gcc aca aca 690
Tyr Pro Gly Cys Pro Tyr Pro Pro Gly Gly Pro Tyr Pro Ala Thr Thr
185                 190                 195                 200

agt tct cag tac cct tct cag cct cct gtg acc act gtt ggt ccc agt 738
Ser Ser Gln Tyr Pro Ser Gln Pro Pro Val Thr Thr Val Gly Pro Ser
                205                 210                 215

agg gat ggc aca atc agc gag gac acc atc cga gcc tct ctc atc tct 786
Arg Asp Gly Thr Ile Ser Glu Asp Thr Ile Arg Ala Ser Leu Ile Ser
            220                 225                 230

gcg gtc agt gac aaa ctg aga tgg cgg atg aag gag gaa atg gat cgt 834
Ala Val Ser Asp Lys Leu Arg Trp Arg Met Lys Glu Glu Met Asp Arg
        235                 240                 245

gcc cag gca gag ctc aat gcc ttg aaa cga aca gaa gaa gac ctg aaa 882
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Ala Gln Ala Glu Leu Asn Ala Leu Lys Arg Thr Glu Glu Asp Leu Lys
    250                 255                 260

aag ggt cac cag aaa ctg gaa gag atg gtt acc cgt tta gat caa gaa   930
Lys Gly His Gln Lys Leu Glu Glu Met Val Thr Arg Leu Asp Gln Glu
265                 270                 275                 280

gta gcc gag gtt gat aaa aac ata gaa ctt ttg aaa aag aag gat gaa   978
Val Ala Glu Val Asp Lys Asn Ile Glu Leu Leu Lys Lys Lys Asp Glu
                285                 290                 295

gaa ctc agt tct gct ctg gaa aaa atg gaa aat cag tct gaa aac aat   1026
Glu Leu Ser Ser Ala Leu Glu Lys Met Glu Asn Gln Ser Glu Asn Asn
            300                 305                 310

gat atc gat gaa gtt atc att ccc aca gct ccc tta tac aaa cag atc   1074
Asp Ile Asp Glu Val Ile Ile Pro Thr Ala Pro Leu Tyr Lys Gln Ile
        315                 320                 325

ctg aat ctg tat gca gaa gaa aac gct att gaa gac act atc ttt tac   1122
Leu Asn Leu Tyr Ala Glu Glu Asn Ala Ile Glu Asp Thr Ile Phe Tyr
    330                 335                 340

ttg gga gaa gcc ttg aga agg ggc gtg ata gac ctg gat gtc ttc ctg   1170
Leu Gly Glu Ala Leu Arg Arg Gly Val Ile Asp Leu Asp Val Phe Leu
345                 350                 355                 360

aag cat gta cgt ctt ctg tcc cgt aaa cag ttc cag ctg agg gca cta   1218
Lys His Val Arg Leu Leu Ser Arg Lys Gln Phe Gln Leu Arg Ala Leu
                365                 370                 375

atg caa aaa gca aga aag act gcc ggt ctc agt gac ctc tac tga       1263
Met Gln Lys Ala Arg Lys Thr Ala Gly Leu Ser Asp Leu Tyr  *
            380                 385                 390

cttctctgat accagctgga ggttgagctc ttcttaaagt attcttctct tccttttatc 1323
agtaggtgcc cagaataagt tattgcagtt tatcattcaa gtgtaaaata ttttgaatca 1383
ataatatatt ttctgttttc ttttggtaaa gactggcttt tattaatgca ctttctatcc 1443
tctgtaaact ttttgtgctg aatgttggga ctgctaaata aaatttgttt t          1494

(SEQ ID NO:4)
Met Ala Val Ser Glu Ser Gln Leu Lys Lys Met Val Ser Lys Tyr Lys
 1               5                  10                  15
Tyr Arg Asp Leu Thr Val Arg Glu Thr Val Asn Val Ile Thr Leu Tyr
            20                  25                  30
Lys Asp Leu Lys Pro Val Leu Asp Ser Tyr Val Phe Asn Asp Gly Ser
        35                  40                  45
Ser Arg Glu Leu Met Asn Leu Thr Gly Thr Ile Pro Val Pro Tyr Arg
    50                  55                  60
Gly Asn Thr Tyr Asn Ile Pro Ile Cys Leu Trp Leu Leu Asp Thr Tyr
65                  70                  75                  80
Pro Tyr Asn Pro Pro Ile Cys Phe Val Lys Pro Thr Ser Ser Met Thr
                85                  90                  95
Ile Lys Thr Gly Lys His Val Asp Ala Asn Gly Lys Ile Tyr Leu Pro
            100                 105                 110
Tyr Leu His Glu Trp Lys His Pro Gln Ser Asp Leu Leu Gly Leu Ile
        115                 120                 125
Gln Val Met Ile Val Val Phe Gly Asp Glu Pro Pro Val Phe Ser Arg
    130                 135                 140
Pro Ile Ser Ala Ser Tyr Pro Pro Tyr Gln Ala Thr Gly Pro Pro Asn
145                 150                 155                 160
Thr Ser Tyr Met Pro Gly Met Pro Gly Gly Ile Ser Pro Tyr Pro Ser
                165                 170                 175
Gly Tyr Pro Pro Asn Pro Ser Gly Tyr Pro Gly Cys Pro Tyr Pro Pro
            180                 185                 190
Gly Gly Pro Tyr Pro Ala Thr Thr Ser Ser Gln Tyr Pro Ser Gln Pro
        195                 200                 205
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Pro Val Thr Thr Val Gly Pro Ser Arg Asp Gly Thr Ile Ser Glu Asp
    210                 215                 220
Thr Ile Arg Ala Ser Leu Ile Ser Ala Val Ser Asp Lys Leu Arg Trp
225                 230                 235                 240
Arg Met Lys Glu Glu Met Asp Arg Ala Gln Ala Glu Leu Asn Ala Leu
                245                 250                 255
Lys Arg Thr Glu Glu Asp Leu Lys Lys Gly His Gln Lys Leu Glu Glu
            260                 265                 270
Met Val Thr Arg Leu Asp Gln Glu Val Ala Glu Val Asp Lys Asn Ile
        275                 280                 285
Glu Leu Leu Lys Lys Lys Asp Glu Glu Leu Ser Ser Ala Leu Glu Lys
    290                 295                 300
Met Glu Asn Gln Ser Glu Asn Asn Asp Ile Asp Glu Val Ile Ile Pro
305                 310                 315                 320
Thr Ala Pro Leu Tyr Lys Gln Ile Leu Asn Leu Tyr Ala Glu Glu Asn
                325                 330                 335
Ala Ile Glu Asp Thr Ile Phe Tyr Leu Gly Glu Ala Leu Arg Arg Gly
            340                 345                 350
Val Ile Asp Leu Asp Val Phe Leu Lys His Val Arg Leu Leu Ser Arg
        355                 360                 365
Lys Gln Phe Gln Leu Arg Ala Leu Met Gln Lys Ala Arg Lys Thr Ala
    370                 375                 380
Gly Leu Ser Asp Leu Tyr
385                 390
```

The specification describes at page 15, lines 4-10, the isolation of proteins encoded by the TSG101 coding sequence, and particularly at page 15, lines 9-10, that they may be "free of other proteins, as well as cellular debris".

## VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

**I.** Claims 29 and 30 have been rejected under 35 U.S.C. 102(b) as anticipated by Genbank Accession number U8213, June 4, 1998.

**II.** Claims 29-30 have been rejected under 35 U.S.C. 102(b) as anticipated by U.S. Patent No. 5,892,016, Brie et al., as teaching an isolated protein identical to the instant SEQ ID NO:4.

## VII. ARGUMENT

The pending rejections in the instant case are based on Appellants' claim to priority. It is not disputed that the cited references, Genbank Accession number U8213 and U.S. Patent No. 5,892,016, teach a polypeptide having the sequence set forth in SEQ ID NO:4. Both references are available as of the filing date of the immediate application, that is October 29, 2003; and both references are not available as references at the time Appellants' priority applications were filed. The Examiner has asserted that the disclosure in the priority document disclosure of SEQ ID NO:4 does not provide support for Appellants' SEQ ID NO:14. Applicants assert that, in view of the

claimed polypeptide, amino acid residues 11-390 of SEQ ID NO:4, being identical in sequence to the previously filed polypeptide, that the requirements for priority are met.

As a factual matter, Appellants have provided below an alignment of SEQ ID NO:4 from the priority document, U.S. Patent no. 5,891,668, having a filing date of June 13, 1996 (upper query sequence) with the presently claimed polypeptide, SEQ ID NO:4, residues 11-390 (lower subject sequence). It can readily be observed that, in fact, the sequences are completely identical.

```
Score =  781 bits (2018),  Expect = 0.0, Method: Compositional matrix adjust.
 Identities = 380/380 (100%), Positives = 380/380 (100%), Gaps = 0/380 (0%)

Query  1    MVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIPVPYRGNTYNI  60
            MVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIPVPYRGNTYNI
Sbjct  11   MVSKYKYRDLTVRETVNVITLYKDLKPVLDSYVFNDGSSRELMNLTGTIPVPYRGNTYNI  70

Query  61   PICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV  120
            PICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV
Sbjct  71   PICLWLLDTYPYNPPICFVKPTSSMTIKTGKHVDANGKIYLPYLHEWKHPQSDLLGLIQV  130

Query  121  MIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPY  180
            MIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPY
Sbjct  131  MIVVFGDEPPVFSRPISASYPPYQATGPPNTSYMPGMPGGISPYPSGYPPNPSGYPGCPY  190

Query  181  PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRWRMKEEMDRAQ  240
            PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRWRMKEEMDRAQ
Sbjct  191  PPGGPYPATTSSQYPSQPPVTTVGPSRDGTISEDTIRASLISAVSDKLRWRMKEEMDRAQ  250

Query  241  AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE  300
            AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE
Sbjct  251  AELNALKRTEEDLKKGHQKLEEMVTRLDQEVAEVDKNIELLKKKDEELSSALEKMENQSE  310

Query  301  NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ  360
            NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ
Sbjct  311  NNDIDEVIIPTAPLYKQILNLYAEENAIEDTIFYLGEALRRGVIDLDVFLKHVRLLSRKQ  370

Query  361  FQLRALMQKARKTAGLSDLY  380
            FQLRALMQKARKTAGLSDLY
Sbjct  371  FQLRALMQKARKTAGLSDLY  390
```

The Examiner has asserted that because the sequence in the present application contains an additional 10 amino acid acids, it is a different product. As stated in the Final Office Action at page 5, the Examiner asserts "one skilled in the art would not recognize the structure of instant SEQ ID NO:4 protein was disclosed in the earlier specification". Appellants respectfully submit that this is a clear error.

Given that the two amino acid sequence are completely identical, and have been consistently referenced in the specification, one of skill in the art would have no difficulty in determining that they were, in fact, the same protein.

The Examiner has taken the position that the additional 10 amino acids present in the currently filed sequence listing, although not listed in the claims, would render the polypeptide unrecognizable to one of skill in the art.

Appellants submit that those of skill in the art are quite capable of determining that two proteins of identical sequence are the same protein. With respect to the Examiner's assertion that the presence of the 10 amino acid sequence renders the presently claimed polypeptide unrecognizable, Appellants note the discussion in the priority document, for example in U.S. Patent no. 5,891,668, provides for the conjugation of the polypeptide to other proteins as carriers, and incorporates by reference such well-known texts as Sambrook, et al. Molecular Cloning: A Laboratory Manual, CSH Press 1989, pp.14.2-14.33, which provides one of skill in the art methods for fusing the sequence of one polypeptide to another.

Appellants respectfully submit that in view of the 100% amino acid identity between the presently claimed protein and the protein sequence set forth in Appellants priority documents; and in view of the knowledge of one of skill in the art with respect to fusing the sequence of one polypeptide to another, that the requirements for priority are met.

In view of the priority claim made at least to U.S. Patent no. 5,891,668, having a filing date of June 13, 1996, Appellants submit that the cited art, Genbank Accession number U8213, June 4, 1998; and U.S. Patent no. 5,892,016, filed January 23, 1997, are not available as art under U.S. 102, and therefore do not anticipate the presently claimed invention.

The Appellants respectfully request that the rejection of Claims 29-30 be withdrawn, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

The appropriate fee is either attached or authorized. If the Commissioner determines that an additional fee is necessary, the Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-0815.**

Respectfully submitted,
BOZICEVIC, FIELD AND FRANCIS LLP

Date: June 11, 2010

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## VIII. CLAIMS APPENDIX

The claims on appeal are as follows:

29. (previously presented) An isolated polypeptide comprising the sequence of amino acid residues 11-390 of SEQ ID NO:4.

30. (previously presented) A polypeptide comprising the sequence of amino acid residues 11-390 of SEQ ID NO:4, free of other proteins and other cellular debris.

31. (withdrawn) A complex comprising the polypeptide of Claim 29 and an antibody bound thereto.

32. (withdrawn) The complex of Claim 31, wherein said antibody is a monoclonal antibody.

33. (withdrawn) An antibody which binds to the polypeptide of Claim 29, to form the complex of Claim 32.

34. (withdrawn) The antibody of Claim 33, wherein said antibody is a monoclonal antibody.

## IX. EVIDENCE APPENDIX

None.

## X. RELATED PROCEEDINGS APPENDIX

None.